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(54) Title: **ENZYMATICALLY ACTIVATED POLYMERIC DRUG CONJUGATES**

(57) Abstract: The present invention relates to a polymeric drug conjugate with one or more biologically active agents conjugated via an enzymatically cleavable linker to either a regular repeating linear unit comprising a water soluble polymer segment and a multifunctional chemical moiety, or a branched polymer comprising two or more water soluble polymer segments each bound to a common multifunctional chemical moiety, as well as to methods of making such conjugates. The present invention is also directed to pharmaceutical compositions comprising such conjugates and to the use of such conjugates to treat pathological conditions.

WO 00/64486 A3

# INTERNATIONAL SEARCH REPORT

International Application No

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EMBASE, BIOSIS, EPO-Internal, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DATABASE MEDLINE 'Online!  US NATIONAL LIBRARY OF MEDICINE (NLM),  BETHESDA, MD, US;  CALICETI P ET AL: "Preparation and  properties of monomethoxy poly(ethylene  glycol) doxorubicin conjugates linked by  an amino acid or a peptide as spacer."  retrieved from STN  Database accession no. 94000214  XP002156126  abstract  &amp; FARMACO, (1993 JUL) 48 (7) 919-32. ,</p> <p style="text-align: center;">--- -/-</p>	1-89



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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\*A\* document defining the general state of the art which is not considered to be of particular relevance

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\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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\* & \* document member of the same patent family

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International Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NICHIFOR M. ET AL: "Polymeric prodrugs of 5-fluorouracil." JOURNAL OF CONTROLLED RELEASE, (1997) 48/2-3 (165-178). , XP004125853 figures 1-3 ---	1-89
E	WO 00 40203 A (WANG NAI FANG ;LIAO JUN (US); MILSTEIN SAM J (US); SMART JOHN E (U) 13 July 2000 (2000-07-13) claims ---	1
X	WO 92 16555 A (ENZON INC) 1 October 1992 (1992-10-01) claims ---	1,20
Y		1-89
Y	BRINKLEY M: "A BRIEF SURVEY OF METHODS FOR PREPARING PROTEIN CONJUGATES WITH DYES, HAPTENS, AND CROSS-LINKING REAGENTS" BIOCONJUGATE CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY, WASHINGTON, vol. 3, no. 1, 1992, pages 2-13, XP000261480 ISSN: 1043-1802 tables I,II ---	1-89
Y	WO 98 19705 A (SQUIBB BRISTOL MYERS CO) 14 May 1998 (1998-05-14) claims ---	1-89
A	EP 0 838 224 A (KURARAY CO) 29 April 1998 (1998-04-29) claims ---	1-89
A	EP 0 712 635 A (KURARAY CO) 22 May 1996 (1996-05-22) claims 1-3 -----	

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

Present claims 1-89 relate to an extremely large number of possible compounds and methods. In fact, the claims contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely those compounds and methods recited in the examples and closely related homologous compounds.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern. Application No

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